Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 35-133 and 152-203 are pending in the application, with claims 35, 44, 53, 62, 73, 75, 81, 83, 90, 92, 99, 108, 117, 127, 152, 160, 168, and 169 being the independent claims. Claims 134-151 are sought to be cancelled without prejudice to or disclaimer of the subject matter therein. Applicants reserve the right to pursue the subject matter of these claims in related applications. Claims 180-203 are sought to be added. These changes are believed to introduce no new matter, and their entry is respectfully requested.

The Office Action Summary (page 1 of Paper No. 1203) lists claims 160-167 as being "rejected." However, the remainder of the office action does not detail any statutory basis for the rejection of these claims. While Applicants believe these claims, as well as all of the pending claims, are in order for allowance, clarification as to the status of claims 160-167 is respectfully requested.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Interview with the Examiner

Applicants thank Examiners Kaufman, Eyler, and Caputa for the courtesy extended in the interview with Applicants' representatives Kenley Hoover, Michele

Wales and Eric Steffe on April 22, 2004. Pursuant to MPEP § 713.04, the substance of the interview as it pertains to the pending claims of the present application was a discussion of possible arguments and/or amendments to overcome the pending rejection under 35 U.S.C. § 102(e) over U.S. Patent No. 6,072,047 ("the '047 patent"). Exhibits shown included a receptor family structure diagram, and molecular weight and sequence comparisons of various TRAIL-binding proteins. No agreement was reached at the interview.

Claim Interpretation

The Examiner has interpreted the phrase "an isolated polypeptide comprising an amino acid sequence . . ." to refer to a contiguous amino acid sequence, which may include additional amino acid sequence on either end. Paper No. 1203 at p. 2. Applicants do not disagree with this interpretation. Given this interpretation, the Examiner points out that Applicants claims to "a polypeptide comprising amino acids 1 to 133 of SEQ ID NO:2," *e.g.*, currently pending claims 160 to 167, would not read on the TRAIL-R receptor sequence disclosed in the '047 patent.

Rejections under 35 U.S.C. § 112

The Examiner has rejected claims 134-135, 137-144, and 146-151 under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. Solely to advance prosecution, and not in acquiescence to the Examiner's rejection, claims 134-135, 137-144, and 146-151 have been canceled, rendering this rejection moot. According, Applicants respectfully request that this rejection be withdrawn.

Rejection under 35 U.S.C. § 102

The Examiner has rejected claims 35, 36, 38, 39, 43-45, 47, 48, 52-54, 56, 57, 61, 73-77, 81-85, 89-94, 98-100, 102, 103, 107-109, 111, 112, 116, 127-129, 133-138, 142-147, 151-155, 159, 168-174, 178, and 179 under 35 U.S.C. § 102(e)[1] as allegedly being anticipated by the '047 patent.

Solely to advance prosecution, and not in acquiescence to the Examiner's rejection, claims 134-138, 142-147, and 151 have been canceled, rendering the rejection moot as to these claims. With respect to the pending claims, Applicants respectfully traverse.

The Examiner argues that the '047 patent "receives priority back to March 12, 1997...for a TRAIL-R that was isolated from human Jurkat cells and human PS-1 cells." Paper No. 1203 at page 4. Applicants respectfully disagree.

The '047 patent claims priority under 35 U.S.C. § 120 back to February 13, 1997 ("PD-1"), through four continuation-in-part applications filed on March 12, 1997 ("PD-2"), March 28, 1997 ("PD-3"), June 4, 1997, and June 26, 1997. As discussed at the April 22 interview and as explained below, PD-1 and PD-2 provide an incomplete and incorrect description of the DR5 polypeptide.

---

[1] The Examiner states that "[t]he changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. § 122(b). Therefore this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA...." Paper No. 1203 at page 3. Applicants respectfully disagree. First, Applicants point out that the present application was filed on December 7, 2001, and in fact published as U.S. Patent Application Publication US 2002-0098550 A1 on July 25, 2002. Second, Applicants note that all pending applications, regardless of their filing date or publication status, should be examined under 102(e) as amended by the AIPA. *See* MPEP § 2136 ("[r]evised 35 U.S.C. 102(e)...applies in the examination of all applications, whenever filed....").

PD-1, filed on Feb. 13, 1997 describes TRAIL-binding polypeptide fractions obtained from solublized Jurkat cells via affinity chromatography with TRAIL. The only "characterization" of a TRAIL binding protein disclosed in PD-1 was: (a) a functional property, the ability to bind TRAIL; (b) a major ("about 52 kD") and a minor ("about 42 kD") band on a denaturing polyacrylamide gel that was obtained by solubilizing surface biotinylated Jurkat cell membranes, and precipitating those proteins present in the preparation that bind TRAIL; and (c) three tryptic peptide sequences, one from Jurkat cell-derived material, and two from PS-1[2] cell-derived material. Of these peptide sequences, only one (VPANEGD) turns out to be a sequence that is found in DR5.

In PD-2, filed March 12, 1997, the peptide sequences from PD-1, including the two sequences not found in DR5, were carried over. PD-2 further disclosed the sequence of a short DNA fragment from the intracellular domain of DR5, and the deduced amino acid sequence of this fragment which corresponds to a non-functional polypeptide fragment. According to PD-2, the degenerate PCR primers used to isolate this fragment were designed based on additional undisclosed tryptic peptide sequences. *See* PD-2 at Example 3.

The TRAIL-binding fractions described in PD-1 and PD-2 were obtained from a Jurkat cell line or PS-1 cell line. Jurkat cells have been reported to express 3 other TRAIL receptors in addition to DR5 (TRAIL-R1, TRAIL-R3, and OPG) (*see* Exhibits B and C below and Fiumara, P. *et al.*, *Blood 98*:2784-2790 (2001), attached hereto as

---

[2] PS-1 cells are described in PD-1 and PD-2 as being "a human B cell line that spontaneously arose after lethal irradiation of human perpheral blood lymphocytes (PBLs). This cell line is not available commercially, and therefore, one of ordinary skill in the art could not easily reproduce these experiments.

Exhibit A). Each of these TRAIL-binding polypeptides have observed molecular weights which could easily correspond to either the major or minor protein band disclosed in PD-1 and PD-2. For example, the observed molecular weight of TRAIL-R1 (DR4) as expressed in Jurkat cells has been reported to be about 57 kD (see catalog entry for "Anti-DR4" from ProSci, Poway, CA, attached hereto as Exhibit B), the observed molecular weight of TRAIL-R3 as expressed in Jurkat cells is reported to be about 32-35 kD (*see* catalog entry for "Anti-TRAIL Receptor 3, N-terminal (73-102) Human" from Calbiochem, attached hereto as Exhibit C), and the observed molecular weight of OPG is reported to be about 55 kD (*see* catalog entry for "Monoclonal Antibody to Human Osteoprotegerin" from Imgenex, San Diego, CA, attached hereto as Exhibit D). Finally, DR5, as described in the present invention, is reported to have an observed molecular weight of about 56 kD and the suggested control cells are Jurkat cells (*see* catalog entry for "Mouse (Monoclonal) Anti-Human DR5 Unconjugated" from Biosource, Camarillo, CA, attached hereto as Exhibit E).

Given the ambiguity and uncertainty regarding the polypeptide(s) described in PD-1 and PD-2, it is apparent that at the time of the first two priority documents, the inventors had not fully characterized any one TRAIL binding protein, let alone DR5. Accordingly, it is clear that the inventors had, at best, described only a partially characterized mixture of different TRAIL-binding polypeptides in PD-1 and PD-2. Since PD-1 and PD-2 do not adequately describe the isolated DR5 protein claimed in the present application, these documents cannot anticipate the pending claims.

Based on these remarks, Applicants respectfully request that the pending 35 U.S.C. § 102(e) rejection of claims 35, 36, 38, 39, 43-45, 47, 48, 52-54, 56, 57, 61, 73-

77, 81-85, 89-94, 98-100, 102, 103, 107-109, 111, 112, 116, 127-129, 133-138, 142-147, 151-155, 159, 168-174, 178, and 179 over the '047 patent be reconsidered, and further that it be withdrawn.

Rejections under 35 U.S.C. § 103

The Examiner has rejected claims 40-42, 49-51, 58-60, 78-80, 86-88, 95-97, 104-106, 113-115, 130-132, 139-141, 148-150, 156-158, and 175-177 under 35 U.S.C. § 103(a) as allegedly being unpatentable over the '047 patent.

Solely to advance prosecution, and not in acquiescence to the Examiner's rejection, claims 139-141 and 148-150 have been canceled, rendering the rejection moot as to these claims. With respect to the pending claims, Applicants respectfully traverse.

As discussed in detail above, PD-1 and PD-2 only described, at best, a partially characterized *mixture* of TRAIL-binding polypeptides from Jurkat or PS-1 cells. Individual species of TRAIL-binding polypeptides, including DR5, were insufficiently characterized and described to render obvious any one species.

Based on these remarks, Applicants respectfully request that the pending 35 U.S.C. § 103(a) rejection of claims 40-42, 49-51, 58-60, 78-80, 86-88, 95-97, 104-106, 113-115, 130-132, 139-141, 148-150, 156-158, and 175-177 over the '047 patent be reconsidered, and further that it be withdrawn.

Other Matters

Claims 41, 42, 50, 51, 59, 60, 70, 71, 74, 79, 80, 87, 88, 96, 97, 105, 106, 114, 115, 124, 125, 131, 132, 157, 158, 165, 166, 176, and 177 have been amended to correct

typographical errors. These amendments do not introduce new matter, and their entry is respectfully requested.

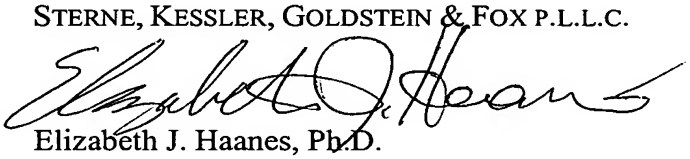
Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



Elizabeth J. Haanes, Ph.D.
Attorney for Applicants
Registration No. 42,613

Date: May 24, 2004

1100 New York Avenue, N.W.
Washington, D.C. 20005-3934
(202) 371-2600